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FreeStyle Libre

THE sensor report

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WELCOME TO
THE SENSOR REPORT, ISSUE 1, 2023

With this first 2023 issue of *The Sensor Report*, we are able to update you with news of recent clinical trial outcomes and substantial real-world data on how the FreeStyle Libre system has demonstrated its efficacy and impact on outcomes for people with type 1 diabetes (T1DM) or type 2 diabetes (T2DM). These include the FLASH-UK randomized controlled trial (RCT) of the FreeStyle Libre 2 sensor in people with T1DM and the RELIEF study data on hospital admissions for acute diabetes events (ADEs) in people with T1DM or T2DM.

The FLASH-UK trial is the first RCT to compare glycemic outcomes for people with T2DM using the FreeStyle Libre 2 system versus usual care with self-monitored blood glucose (SMBG) testing. The RELIEF study is notable for using the French national health claims database, which covers the entire French population and includes exhaustive information on all healthcare resource use, at an individual level. The data from the retrospective longitudinal RELIEF study represent the largest investigation to date of the impact of using the FreeStyle Libre system on rates of hospitalization for ADEs, such as diabetic ketoacidosis and severe hypoglycemia.

Furthermore, using the FreeStyle libre system or traditional CGM is increasingly being associated with outcomes in addition to glucose metabolism, underscoring the value of these technologies in the management of people with diabetes, particularly for improved healthcare-related quality of life (HRQoL). In this Issue of *The Sensor Report* we provide insights from recent studies that shed light on these important topics.

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featurestory

Independent RCT in people with T1DM using Freestyle Libre 2 system significantly improves glycemic outcomes over 24 weeks compared to SMBG

In their introduction to this study, published in the *New England Journal of Medicine*, the investigators of the FLASH-UK randomised controlled trial (RCT) note the lack of RCT data to assess the efficacy of the system, an economic evaluation of the relative costs and benefits of the system, or an assessment of patient acceptability[1]. Therefore, the investigators set out to establish whether use of the FreeStyle Libre 2 flash glucose monitoring system, with optional alarms for low and high glucose, would affect glycaemic control in adults with type 1 diabetes (T1DM).

The FLASH-UK multi-centre, open-label, two arm, parallel, study is the first RCT of the FreeStyle Libre 2 system in people with T1DM. The primary aim of the study was to evaluate the impact of FreeStyle Libre 2 use over 6 months in this population to improve HbA1c compared with usual care with self-monitoring of blood glucose (SMBG). Secondary outcomes included sensor-based metrics such as time in ranges, insulin dose changes, adverse events and user reported psychosocial measures. The user experience of FSL 2 and cost effectiveness were also explored and will be published separately.[1]

The FLASH-UK RCT was conducted in primary and secondary care sites and included 156 individuals aged 16 years or older, with T1DM treated by either multiple daily insulin injections or insulin pump therapy, and with an HbA1c 7.5% - 11% (59 to 97mmol/mol). Study participants

were randomised 1:1 to either the intervention or control arm and their glycaemic management was reviewed at 4, 12 and 24 weeks[1].

Mean baseline HbA1c levels were 8.7% (72 mmol/mol) in the intervention group and 8.5% (69 mmol/mol) in the usual-care group; these levels decreased to 7.9% (63 mmol/mol) and 8.3% (67%), respectively, at 24 weeks, an adjusted mean difference of -0.5% in the intervention group ($p<0.001$). Time in range (TIR) 3.9-10.0 mmol/L (70-180 mg/dL) was increased by 9.0 percentage points (130 mins) in the FreeStyle Libre 2 system user group than in the SMBG group, and time below range <3.9 mmol/L (<70 mg/dL) was reduced by 3.0 percentage points (43 mins) in the intervention group. This translates into an additional 130 mins/day in TIR, 43 mins/day less in hypoglycemia and 86 mins/day less time in a hyperglycemic state.

Participant-reported outcome measures (PROMs) revealed that using the FreeStyle Libre 2 system with optional alarms resulted in a higher total diabetes treatment satisfaction (DTSQ) score in the intervention group than in the SMBG group, and the glucose monitoring satisfaction survey (GMSS) score was also higher in the intervention group than in the SMBG group. These results reflect the greater overall satisfaction of the FreeStyle Libre 2 system users and that the device was easy to use and that it functioned well and accurately.

1. Leelarathna L, et al. Intermittently Scanned Continuous Glucose Monitoring for Type 1 Diabetes *N Engl J Med.* 2022;387(16):1477-1487. doi: 10.1056/NEJMoa2205650

Image for illustrative purposes only. Not real patient.

Flash glucose monitoring is associated with RELIEF from acute diabetes events and hospital admissions

For people with type 1 diabetes (T1DM) or type 2 diabetes (T2DM) on insulin therapy, poor glucose control can lead to acute diabetes events (ADEs), including severe hypoglycemia, severe hyperglycemia and diabetic ketoacidosis (DKA). Although such ADEs can be prevented by frequent glucose monitoring, hospital admissions for these ADEs are increasing and are associated with significant healthcare expenditure[1-6].

The FreeStyle Libre flash glucose monitoring system was approved for reimbursement in France in June 2017 for people with T1DM or T2DM treated with insulin. Using the SNDS national dataset (see inset), the RELIEF study has been able to assess longitudinal hospitalization rates for ADEs in France, before and after initiating flash glucose monitoring with the FreeStyle Libre system.

Image for illustrative purposes only. Not real patient or healthcare provider.

The significance of the RELIEF outcomes

The RELIEF study outcomes use data extracted from the French national health claims database, the Système National des Données de Santé (SNDS) which covers the entire French population (approx. 66 million people) and includes exhaustive information on all healthcare resource use, including diagnosis of acute and chronic conditions, outpatient visits, hospital admission and procedures, dispensed medication and date of death, on an individual level.

Impact of FreeStyle Libre system on ADEs and hospital admissions

In the first of a series of retrospective cohort studies[7], the RELIEF study identified 74,011 adults with T1DM or T2DM from the SNDS dataset who initiated the FreeStyle Libre system during the study period. Hospitalizations for DKA, severe hypoglycemia, diabetes-related coma and hyperglycemia were recorded for the 12 months before and after initiation.

Compared to the 12 months prior to starting the FreeStyle Libre system, hospitalizations for ADEs fell by -49.0% in T1DM and by -39.4% in T2DM in the year after FreeStyle Libre initiation. Admissions for DKA fell in T1DM by -56.2% in T1DM and by -52.1% in T2DM. Before initiation of the FreeStyle Libre system, hospitalizations were most marked

for people who were non-adherent with self-monitored blood glucose (SMBG) testing (0 tests/day), and for those with most use of SMBG (>5 tests/day), which fell by -54.0% and -51.2% respectively following FreeStyle Libre initiation.

Reductions in ADEs with FreeStyle Libre system are sustained for at least 2 years

A follow-up analysis[8] revealed that the reductions in ADEs evident at 12 months after initiating flash glucose monitoring were persistent at 24 months, compared to the 12 months prior to starting. In the 2 years after initiation of the FreeStyle Libre system, hospitalizations for ADEs were reduced by -49% in adults with T1DM and by -48% in T2DM, driven by reductions in DKA. After 2 years, 88% of users persisted with flash glucose monitoring and estimated use of SMBG strips had reduced by -82% and by -84% in adults with T1DM or T2DM, respectively.

Hospitalization for ADEs are also reduced in people with T2DM on basal insulin therapy

The RELIEF study data also included 5933 adults with T2DM on basal insulin therapy who started the Freestyle Libre system during the selection period[9]. Amongst this group, the rate of hospitalizations for ADEs was reduced by -67% as compared to the year before FSL initiation. This reduction in ADEs was driven by 75% fewer DKA admissions, with a -44% reduction in admissions for severe hypoglycemia. The patterns of reduction in ADEs persisted after 2 years.

The RELIEF study is the largest investigation to date on the impact of flash glucose monitoring on rates of hospitalization for ADEs. It shows that initiating the FreeStyle Libre system is associated with considerable reductions in hospital admissions for DKA, severe hypoglycemia and diabetes-related coma in T1DM, T2DM on intensive or non-intensive insulin therapy. The RELIEF study outcomes have clear implications for the use of the FreeStyle Libre system for patient-centered diabetes care and for long-term health economic outcomes.

1. Zhong VW, et al. Incidence and trends in hypoglycemia hospitalization in adults with Type 1 and Type 2 Diabetes in England, 1998–2013: A retrospective cohort study. *Diabetes Care* 2017; 40: 1651–1660.
2. Parekh WA, et al. Approach to assessing the economic impact of insulin-related hypoglycaemia using the novel Local Impact of Hypoglycaemia Tool. Diabet Med 2015; 32: 1156–1166.
3. Kitabchi AE, et al. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care* 2009;32: 1335–1343
4. Zhong VW, et al. Trends in hospital admission for diabetic ketoacidosis in adults with Type 1 and Type 2 Diabetes in England, 1998–2013: A retrospective cohort study. *Diabetes Care* 2018; 41: 1870–1877
5. Dhatariya KK, et al. The cost of treating diabetic ketoacidosis in the UK: a national survey of hospital resource use. *Diabet Med* 2017; 34: 1361–1366.
6. Benoit SR, et al. Trends in Emergency Department Visits and Inpatient Admissions for Hyperglycemic Crises in Adults With Diabetes in the US. 2006–2015. *Diabetes Care* 2020; 43: 1057-1064 doi: 10.2337/dc19-2449
7. Roussel R, et al. Important Drop in Rate of Acute Diabetes Complications in People With Type 1 or Type 2 Diabetes After Initiation of Flash Glucose Monitoring in France: The RELIEF Study. *Diabetes Care* 2021; 44:1368-1376. doi: 10.2337/dc20-1690
8. Riveline J-P, et al. Reduced Rate of Acute Diabetes Events with Flash Glucose Monitoring Is Sustained for 2 Years After Initiation: Extended Outcomes from the RELIEF Study. *Diabetes Technol Ther.* 2022; 24:611-618. doi: 10.1089/dia.2022.0085
9. Guerci B, et al. Important Decrease in Hospitalizations for Acute Diabetes Events Following FreeStyle Libre System Initiation in People with Type 2 Diabetes on Basal Insulin Therapy in France. *Diabetes Technol Ther.* 2023; 25:20-30. doi: 10.1089/dia.2022.0271

researchupdates

Introduction of alarms in the FreeStyle Libre 2 system increases time in range, reduces hypoglycemia and improves quality of life

This prospective observational study assessed the impact of using the FreeStyle Libre 2 system on metabolic outcomes and sleep on children and adolescents with T1DM.

The study recruited 47 children and adolescents with T1DM who had experience using the FreeStyle Libre system without alarms and switched them to using the FreeStyle Libre 2 system with alarms for 14 days. The study involved complete psychosocial and sleep-related questionnaires of the enrolled children and adolescents, as well as their caregivers, along with wearing an actigraph to measure sleep quality, whose readings were processed by the certified algorithm “Dormi”.

The study found that switching to the FreeStyle Libre 2 system led to a 5 percent increase in time in range 3.9-10.0 mmol/L (70-180 mg/dL), a reduction in time below range <3.9 mmol/L (70 mg/dL), reduced frequency of hypoglycemic events, and lower glycemic variation. Furthermore, the introduction of optional alarms did not affect sleep duration or quality, either for the FreeStyle Libre 2 system users or their parents. Of note, the switch to the FreeStyle Libre 2 system improved quality of life as perceived by the parents.

Franceschi R, et al. Impact of intermittently scanned continuous glucose monitoring with alarms on sleep and metabolic outcomes in children and adolescents with type 1 diabetes. *Acta Diabetologica* 2022; 59: 911-919. doi:10.1007/s00592-022-01882-3

Image for illustrative purposes only. Not real patient.

Flash glucose monitoring is associated with a decreased rate of depressive disorders among people with diabetes

This FLARE-NL7 study used a series of validated questionnaires to assess whether there was a change in the mental health of people with diabetes after starting the FreeStyle Libre system.

The study included individuals who used the FreeStyle Libre system for 12 months and completed the 12-Item Short Form Health Survey (SF-12) questionnaire at baseline, 6 and 12 months. An SF-12 Mental Component Score (MCS) of ≤45 was used as a cut-off to discriminate respondents with a depressive disorder.

A total of 674 patients were included, 78.2% with T1DM and HbA1c 62.8 mmol/mol (7.9%) at start of the study. At baseline, 235 (34.9%) people had an SF-12 MCS ≤45, which decreased to 30.0% after 6 and 25.7% after 12 months ($p<0.01$ in both cases). Overall, MCS improved from 48.5 at baseline to 50.7 after 6 months and 51.3 after 12 months. In multivariable regression analysis, age and MCS at baseline were associated with improvement of MCS after 12 months of FreeStyle Libre system use.

This analysis suggests that using the FreeStyle Libre system is associated with a decreased rate of depressive disorders among people with diabetes.

Bakker JJ, et al. Commencement of flash glucose monitoring is associated with a decreased rate of depressive disorders among persons with diabetes (FLARE-NL7). *BMJ Open Diabetes Research and Care*. 2022: 10: e002769.

Budget impact analysis of the FreeStyle Libre system for type 1 diabetes patients in the UK

A budget impact analysis was developed using the data collected in the Association of British Clinical Diabetologists (ABCD) FreeStyle Libre Nationwide Audit of people with T1DM using the FreeStyle Libre system.

The cost incurred when a T1DM population (n=1,790) using self-monitoring of blood glucose (SMBG) was compared to the cost for a scenario with increased use of the FreeStyle Libre system. Data collected from the ABCD Nationwide Audit was used to create a budget impact model to estimate the impact of increased SMBG.

The analysis showed that using the FreeStyle Libre system reduces resource utilization in managing T1DM. Initial higher acquisition costs are offset by the healthcare costs avoided in the longer term, with a difference of £168 per patient per year (PPPY). Total costs stood at £1,116 PPPY for using the FreeStyle Libre system and £948 PPPY for SMBG. In local UK health economy settings, an increase from 30% to 50% of FreeStyle Libre system use increases costs by 3.4% (£1,787,345 – £ 1,847,618) and a further 3.3% when increased to 70%.

This increased cost is offset by the numerous system benefits that result from the use of this technology, including access to several glucose metrics that can substitute for quarterly HbA1c blood tests, as well as enabling remote consultation and monitoring of people with T1DM. The cost savings from reduced HbA1c with the FreeStyle Libre system are projected to be greater for people with T1DM and a high HbA1c baseline (>8.5%), relative to the overall population.

The authors conclude that the widespread adoption of the FreeStyle Libre system in people with T1DM offers numerous benefits and has a relatively small budget impact, compared with the total cost of glucose management to health economies in the UK. People with T1DM and healthcare systems stand to benefit from improved glycemic control, reduced diabetes-related distress, reduced hospital admissions, as well as the opportunity for telemonitoring and telemedicine that are provided by using the FreeStyle Libre system.

Blissett R, et al. FreeStyle Libre Flash Glucose Monitoring system for people with type 1 diabetes in the UK: a budget impact analysis. *BMJ Open Diabetes Research and Care*. 2022; e002580. Doi. 10.1136/bmjdrc-2021-002580

Cost-effectiveness of glucose monitoring for adults with T1DM in Canada: a modelling study

Maintaining healthy glucose levels is critical for the management of T1DM, but the most cost-effective glucose monitoring approach is not clear.

The population-level impact of glucose monitoring systems on diabetes-related complications, mortality, and cost-effectiveness in adults with T1DM in Canada was modelled. Primary outcomes included the number of complications and deaths and the incremental cost-effectiveness ratio (ICER) of flash glucose monitoring relative to usual care with self-monitored blood glucose (SMBG).

An initial cohort of 180,000 with baseline HbA1c of 8.1% was used to represent all Canadians aged 18-64 years with T1DM. Universal use of flash glucose monitoring was associated with approximately 3,400 (1.9% of the cohort) more people living with T1DM free of complications and approximately 4,600 (2.6%) fewer deaths. Universal use of the FreeStyle Libre system in the Canadian T1DM population is anticipated to reduce diabetes-related complications and mortality at an acceptable cost-effectiveness threshold.

Rotondi MA, et al. Population-Level Impact and Cost-effectiveness of Continuous Glucose Monitoring and Intermittently Scanned Continuous Glucose Monitoring Technologies for Adults with Type 1 Diabetes in Canada: A Modeling Study. *Diabetes Care*. 2022; 45(9); 2012-2019.

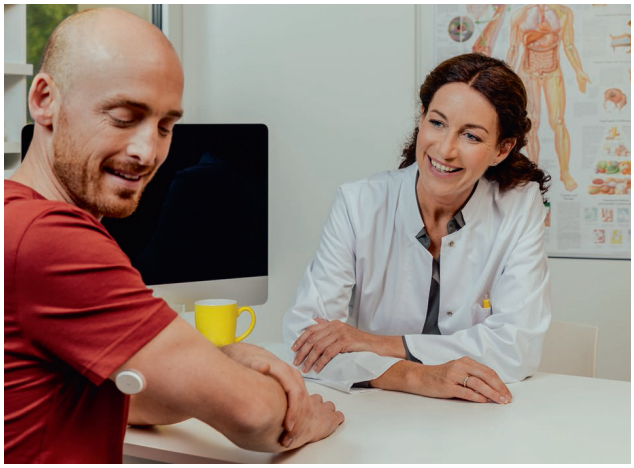

Image for illustrative purposes only. Not real patient.

Periodic short-term use of CGM in non-insulin-treated T2DM can be effective in reducing HbA1c

This study evaluated the efficacy of intermittent short-term use of a traditional continuous glucose monitoring (CGM) system in adults with T2DM uncontrolled with oral antidiabetic drugs.

In this multicenter, randomized prospective study, 61 participants were randomly assigned to treatment group 1 (one session of CGM), treatment group 2 (two sessions of CGM with a 3-month interval between sessions) and a control group. At 3 months, a significant HbA1c reduction was observed in treatment group 1 (-0.60%, p=0.044) and treatment group 2 (-0.64%, p=0.014) compared with the control group. Especially in the treatment groups, individuals performing self-monitoring of blood glucose (SMBG) at least 1.5 times/day showed a significant HbA1c improvement, at both 3 and 6 months, but those performing SMBG less than 1.5 times/day showed no significant improvement. This indicates the value of routine glucose monitoring between periodic applications of CGM.

The outcomes indicate that non-insulin-treated adults with T2DM can benefit from intermittent short-term use of CGM as an effective method for glucose control, especially in those with consistent SMBG behaviour in-between applications of CGM.

Moon SJ, et al. Efficacy of intermittent short-term use of a real-time continuous glucose monitoring system in non-insulin–treated patients with type 2 diabetes: A randomized controlled trial. *Diabetes Obesity Metab.* 2023; 25, 110-120.

Flash glucose monitoring is associated with improvement in HbA1c maintained over 4 years in people with T1DM

This retrospective study aimed to illustrate the long-term effects of using the FreeStyle Libre system in adults with T1DM

Electronic patient records in North Karelia, Finland, were used to identify patients with TD1M over 18 years (n=689) and using the FreeStyle Libre system. Change in mean HbA1c over time was assessed from collected data before and after initiation of flash glucose monitoring.

The study found that the use of isCGM results in significant improvement in HbA1c levels in adults with T1DM, with the greatest reductions occurring after 6 months (-0.54% [-5.9mmol/mol], p<0.001) and 12 months (-0.42% [-4.6mmol/mol], p<0.001). This reduction was sustained over 4 years, but the effect diminished over time, with a mean reduction of -0.18% (-2.05mmol/mol) (p=0.009) at 48 months compared with the baseline. Age and sex had no significant correlation with A1C reduction when isCGM was used. Adults with baseline HbA1c >9% (75mmol/mol) benefited the most from starting flash glucose monitoring, with a mean reduction of -0.97% (-10.6mmol/mol; p<0.001) at 12 months, with a sustained reduction of -0.92% (-10.1mmol/mol; p<0.001) at 48 months.

Mustonen J, et al. Marked Improvement in A1C Levels After Initiation of Intermittently Scanned Continuous Glucose Monitoring Is Maintained Over 4 Years in Patients With Type 1 Diabetes. *Diabetes Spectrum 2022*; doi.org/10.2337/ds21-0087

The effect of flash glucose monitoring on the relationship with food and eating behavior of adults with T1DM

This study provides insights into how dietary and eating behaviors of adults with T1DM can be influenced by the FreeStyle Libre system.

Adults with T1DM using the FreeStyle Libre system participated in interviews on their experiences, their relationship with food and eating habits for a minimum of one year. Fifteen of these interviews were subjected to a reflexive thematic analysis to determine how the FreeStyle Libre system impacts this behavior.

The study found that using the FreeStyle Libre system influences the quantity, type, eating time, and why adults with T1DM consume certain foods. It was clear that using the FreeStyle Libre system increased participants self-awareness of their food consumption. This included their view of the body as a machine needing continuous maintenance, their increased confidence and new discoveries in food choices, before and after diabetes diagnosis, and their shift in expectations in regard to diabetes management.

All these themes had both a positive and negative impact on the overall well-being of patients and their view of their conditions. T1DM is a chronic condition, and food is a major factor influencing the degree of glucose control and quality of life; clinical care should strive to address the patient's relationship with food in routine care alongside using the FSL glucose monitoring system.

Wallace T, et al. The Impact of Flash Glucose Monitoring on Adults with Type 1 Diabetes' Eating Habits and Relationship with Food. *Diabetes Res Clin Pract.* 2022: 110230. doi.org/10.1016/j.diabres.2022.110230

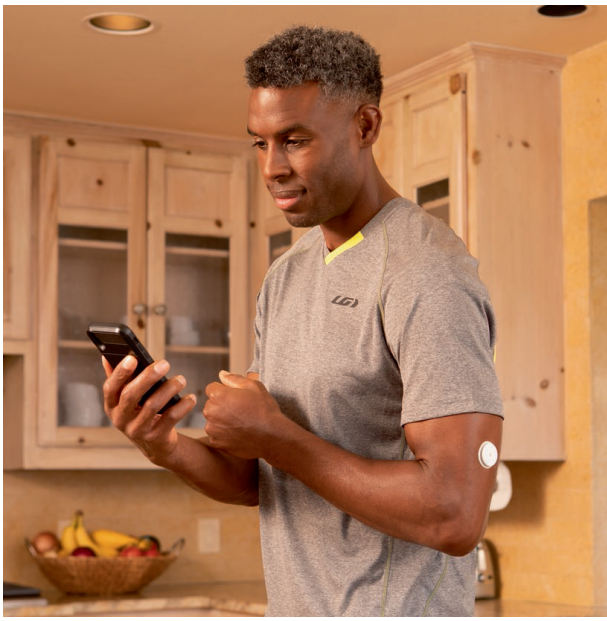

Image for illustrative purposes only. Not real patient.

Using CGM-metrics for evaluating therapeutic efficacy in people with diabetes

The author evaluated correlations among CGM metrics from studies in T1DM and T2DM to test their value as alternatives to HbA1c in assessing therapeutic efficacy.

This analysis reviewed correlations among CGM-derived mean glucose, time in range (TIR) and time above range (TAR), alongside HbA1c, from studies involving 545 people with T1DM, 5,910 people with T2DM and 98 women with T1DM during pregnancy and postpartum.

The author found that mean glucose is correlated more-closely with %TAR (r = 0.98 in T1DM, 0.97 in T2DM) and with %TIR (r = -0.92 in T1D, -0.83 in T2D) than with HbA1c (r = 0.78 in T1D). Furthermore, changes in mean glucose level after six months of traditional CGM use by people with T1DM also showed higher correlations with changes in %TAR (r = 0.95) and %TIR (r = -0.85) than with changes in HbA1c (r = 0.52). Overall, %TAR typically performs better than %TIR as a predictor of mean glucose than HbA1c.

The study concluded that any of the three CGM metrics examined could be used to evaluate the efficacy of a therapeutic intervention intended to reduce average glucose levels. Overall, these CGM metrics, along with metrics of hypoglycemia and glycemic variability, provide a comprehensive assessment of the overall quality of glycemic control and could be considered as criteria for analysis of new therapies..

Rodbard D. Continuous glucose monitoring metrics (Mean Glucose, time above range and time in range) are superior to glycated haemoglobin for assessment of therapeutic efficacy. *Diabetes Obesity Metab.* 2023; 25: 596-601. doi:10.1111/dom.14906

Flash glucose monitoring in people with T2DM on non-insulin therapy: IMMEDIATE study phase 1 outcomes

People with T2DM who are not meeting glycemic goals on non-insulin antihyperglycemic drugs face the prospect of escalation to treatment with insulin. The IMMEDIATE study evaluates the impact of starting flash glucose monitoring on glucose control in this population.

The IMMEDIATE study enrolled 116 adults with T2DM and HbA1c > 7.5% (58 mmol/mol) into a randomized controlled, open-label crossover study. In Phase 1 of the study, participants were randomized to a 16-week intervention with the FreeStyle Libre system, combined with diabetes self-management education (DSME), or a control arm with a 16-week DSME intervention alone.

At the end of 16 weeks, participants in the FreeStyle Libre + DSME arm showed 9.9% greater (2.4 hrs) time in range (TIR) compared to the DSME-only control arm ($p < 0.01$). Similarly, time above range (TAR) was 8.1% (1.9 hrs) lower in the FreeStyle Libre + DSME arm ($p=0.037$). At 16 weeks, HbA1c was reduced by 0.3% (3 mmol/mol) in the FreeStyle Libre + DSME arm ($p=0.048$). Glucose monitoring satisfaction scores improved only in the FreeStyle Libre + DSME arm (0.6 vs. 0.0; $p<0.01$).

This report on the Phase 1 outcomes from the IMMEDIATE study shows that people with T2DM inadequately controlled on non-insulin drugs can achieve significant improvements in HbA1c, TIR and TAR following initiation of the FreeStyle Libre system.

Aronson R, et al. IMpact of flash glucose Monitoring in pEople with type 2 Diabetes Inadequately controlled with non-insulin Antihyperglycemic ThErapy (IMMEDIATE): A Randomized Clinical Trial. *Diabetes Obesity Metab.* 2022; doi: 10.1111/dom.14949

Personalizing the use of the FreeStyle Libre system allows cost-effective application of flash glucose monitoring

The FLARE-NL9 study aimed to identify subgroups of people with T1DM to understand better the real-world cost-effectiveness perspective.

Clinical data on 381 adults with T1DM was taken from a 12-month prospective observational study using the Dutch FLARE-NL registry and linked to insurance records. Health-related quality of life was assessed with the EQ-5D-3L questionnaire. Individuals were categorized into 4 subgroups: (1) frequent hypoglycemic events, (2) HbA1c > 70 mmol/mol (8.5%), (3) an occupation that requires avoiding finger pricks and/or hypoglycemia, and (4) multiple indications. Costs and outcomes for the 12 months before and after initiation of the FreeStyle Libre system were compared, and incremental cost-effectiveness ratios (ICERs) were calculated at the willingness to pay €50,000 per quality-adjusted life year (QALY) gained.

From a societal perspective, use of the FreeStyle Libre system was cost-effective compared to usual care with self-monitored blood glucose (SMBG) testing for all subgroups except those with frequent hypoglycemic events (ie higher healthcare-related quality of life [HRQoL] and lower costs). The most cost-effective subgroup was those with occupation-related avoidance of fingerprick testing. The individuals in this subgroup were younger and had lower HRQoL and costs at baseline, which may explain why they benefited the most.

Emamipor S, et al. Personalizing the Use of a Intermittently Scanned Continuous Glucose Monitoring (isCGM) Device in Individuals With Type 1 Diabetes: A Cost-Effectiveness Perspective in the Netherlands (FLARE-NL 9). *J. Diabetes Sci Technol.* 2022; 19322968221109841. doi: 10.1177/19322968221109841

Image for illustrative purposes only. Not real patient.

LIBERATES trial shows that flash glucose monitoring is an effective intervention in people with T2DM and recent-onset myocardial infarction

The LIBERATES trial analyzed the use of the FreeStyle Libre system compared to self-monitoring of blood glucose (SMBG) on glycemic and patient-reported outcomes in people with T2DM and recent acute myocardial infarction (AMI).

This multicenter two-arm randomized trial included 141 people with T2DM and recent AMI, treated with insulin and/or a sulphonylurea before hospital admission. Outcome measures included time in range (TIR) 3.9-10 mmol/L (70-180 mg/dL) on days 76-90 post randomization, time below range <3.9 mmol/L (70 mg/dL), change in HbA1c, clinical outcome, quality of life (QOL) and cost effectiveness.

Application of the FreeStyle Libre system was associated with increased TIR by 17 min/day, with 59% probability of benefit. Users of the FreeStyle Libre system showed significantly lower hypoglycemic exposure at days 76-90 (-80 min/day), which was also evident at days 16-30 (-28 min/day). Health-related QOL measures marginally favored isCGM, and the intervention proved to have a 100% probability of being cost effective at a threshold of £20,000 per quality-adjusted life year.

These outcomes favour the use of flash glucose monitoring in people with T2DM and recent AMI, however additional studies are required to understand whether these glycemic differences translate into longer-term clinical benefit.

Ajjan RA, et al. Multicenter Randomized Trial of Intermittently Scanned Continuous Glucose Monitoring Versus Self-Monitoring of Blood Glucose in Individuals With Type 2 Diabetes and Recent-Onset Acute Myocardial Infarction: Results of the LIBERATES Trial. *Diabetes Care.* 2022; Dec 14:dc221219. doi: 10.2337/dc22-1219

Normal birth weight is associated with achieving significantly lower mean daily CGM glucose levels during pregnancy in T1DM

This analysis informs clinical care during pregnancy in T1DM by determining gestational changes in CGM glucose metrics and their relationship to birth weight.

The study used more-than 10.5 million CGM measurements from 386 pregnant women with T1DM. CGM glucose metrics and 24-h glucose profiles were calculated for each gestational week, and the relationship to normal for gestational age (NGA; 10-90th percentile) and large for gestational age (LGA; >90th percentile)) birth weight infants.

Mean glucose concentration fell and percentage of time spent in the pregnancy target range of 3.5-7.8 mmol/L (63-140 mg/dL) increased in the first 10 weeks of pregnancy and plateaued until 28 weeks of gestation, before further improvement in mean glucose and percentage of time in target range until delivery. Maternal CGM glucose metrics diverged at 10 weeks of gestation, with significantly lower mean CGM glucose concentration (7.1 mmol/L [128 mg/dL] vs. 7.5 mmol/L [135 mg/dL]) and higher percentage of time in the pregnancy target range (55% vs. 50%) in women who had NGA versus LGA deliveries.

Normal birth weight is associated with achieving significantly lower mean glucose concentration across the 24-h day and higher time in pregnancy target range from before the end of the first trimester, emphasizing the need to use weekly CGM glucose targets for optimizing maternal glycemia from early pregnancy.

Scott EM, et al. Continuous Glucose Monitoring Metrics and Birth Weight: Informing Management of Type 1 Diabetes Throughout Pregnancy. *Diabetes Care* 2022; 45(8):1724-1734. doi: 10.2337/dc22-0078

Image for illustrative purposes only. Not real patient.

Association of flash glucose monitoring with lower spontaneous abortion rate compared with SMBG testing in pregnant women with T1DM

This study compared characteristics in a cohort of pregnant women with type 1 diabetes (T1D) using the FreeStyle Libre system or conventional blood glucose monitoring.

In this observational study that followed a cohort of 153 pregnant women with T1DM, 77 women were using flash glucose monitoring and 76 were using SMBG testing. Maternal characteristics and maternal-fetal complications were compared between the two groups. The level of HbA1c was measured prior to pregnancy and then four times during gestation (after 8-12, 24-28, 30-33, and 35-37 weeks). There were no significant intergroup differences in the obstetric history.

The spontaneous abortion rate was significantly lower in the flash glucose monitoring group than in the SMBG group (5.3% vs. 20%, respectively; p=0.0129), while HbA1c levels were similar during the study to 37 weeks. There were no significant intergroup differences in the incidence of other maternal-fetal complications, such as delivery type, pregnancy term, prematurity, the proportion of scheduled cesarean sections or blood-loss during delivery.

This observational study supports the use of flash glucose monitoring during pregnancy in T1DM as a means of improving obstetric and neonatal outcomes.

Lemaitre M, et al. Intermittently scanned continuous glucose monitoring is associated with lower spontaneous abortion rate compared with conventional blood glucose monitoring in pregnant women with type 1 diabetes: An observational study. *Diab Vasc Dis Res.* 2022; 19(6),14791641221136837.

International consensus on use of CGM devices and CGM metrics for prospective clinical trials

For the first time, an international expert group has provided consensus recommendations on how to optimise CGM-derived glucose data collection in clinical studies, including the specific glucose metrics and specific glucose metrics that should be evaluated.

Prospective and randomized controlled clinical studies in diabetes, especially with newer pharmaceutical agents, can benefit greatly from incorporating CGM devices for both the comparative monitoring of the intervention and as clinically relevant, primary outcome measures that complement established HbA1c outcomes. Additionally, the use of CGM-derived metrics can identify selective treatment targets related to hypoglycemia, postprandial hyperglycemia, and glucose variability. The demonstrated efficacy and safety of CGM devices by themselves to positively impact a range of measures of glycemic control, poses a challenge to effective trial design. Although the use of blinded sensors can minimize the confounding CGM-effect, the use of unblinded CGM must also be accommodated, particularly in T1DM where use of personal GCM devices is now widespread.

In order to optimize study objectives, careful consideration must be given to the selection and use of CGM devices used for data collection. Different attributes of different systems will better suit different study protocols and participant cohorts. Equally, among the diverse range of study endpoints that can be supported by CGM devices, it is critical to select those that have most relevance to the study objectives.

The recommendations agreed by the international consensus group are centred on providing clear guidance on how the use of CGM devices can be most-effectively incorporated into protocols for prospective clinical studies, such that the resulting glucose metrics can be collected, managed and interpreted with confidence in the context of the trial objectives and outcomes. Importantly, the clinical significance of some CGM metrics, such as time below range, needs to be considered according to patient-related outcomes.

Battelino T, et al. Continuous glucose monitoring and metrics for clinical trials: an international consensus statement. *Lancet Diabetes Endocrinol.* 2022;11(1):42-57

Higher daily scan rates correlate with reduced fear of hypoglycemia in adults with T1DM using the FreeStyle Libre system

The study looked at the association of FreeStyle Libre sensor scanning frequency with glycemic indices and fear of hypoglycemia (FOH) in adults with T1DM.

The researchers included 77 adults with T1DM (mean age 34 years) from a single outpatient clinic in Krakow, Poland. Daily scan frequencies were based on their ambulatory glucose profile (AGP) reports from their last 14 days prior to the outpatient visit and their FOH was assessed using the Hypoglycemia Fear Survey II (HFS II) tool.

There was a significant correlation between increased average daily scanning frequency and lower mean glucose and reduced time in hypoglycemia. Notably, FOH was reduced in the higher scanning groups compared to lowest scanning groups, as measured by HFS II scores (30.3 vs 42.5; $p<0.05$).

This study highlights that higher daily sensor scanning frequency with the FreeStyle Libre system is associated not only with better glycemic indices but also with less FOH in adults with T1DM.

Hohendorff J, et al. Higher scanning frequency is correlated with less fear of hypoglycemia in type 1 diabetes patients using isCGM. *Frontiers in endocrinology.* 13 996933. 6 Oct. 2022, doi:10.3389/fendo.2022.996933

Use of the FreeStyle Libre system combined with structured education reduces hypoglycemia in people with T1DM

This randomised, crossover trial used flash glucose monitoring with structured education as compared with standard care with SMBG to reduce hypoglycemia in adults with T1DM.

This crossover trial involved 104 participants with T1DM on multiple daily injections, randomly allocated to intervention with the FreeStyle Libre system plus education or to the control group on usual care. During the 84-day intervention period, participants used the FreeStyle Libre system and received structured education to prevent hypoglycemia based on the trend arrow and by frequent sensor scanning (≥10 times a day). The primary endpoint was change in time below range (TBR; <70 mg/dL) between the study groups.

The researchers found that the intervention group were able to reduce their %TBR to 10.1% (2.42 h/day) compared to the control group (12.9% or 3.10h/day; $p=0.012$). There was also a significant reduction in the ratio of high-risk study participants with low blood glucose index >5 (8.6% vs 23.7%, $p < 0.001$), amongst the intervention group.

ISCHIA Study Group. Prevention of hypoglycemia by intermittent-scanning continuous glucose monitoring device combined with structured education in patients with type 1 diabetes mellitus: A randomized, crossover trial *Diabetes Res Clin Pract.* 2022; 195:110147. doi: 10.1016/j.diabres.2022.110147

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